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# Biochemical consider on the defensive role of Ginseng in male rabbits

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**Abstract**

Ginseng (Panax ginseng C.A. Meyer) roots have been used for a long time as a traditional medicine in Asian countries for preventive and therapeutic purposes. Ginseng has immune-modulatory anti-tumor antioxidant, and glucose-lowering activities. We have therefore investigate the effects of either 100 mg/kg B.W. doses of ginseng on the levels of biochemical parameters in male New Zealand White rabbits. Animals were orally given 100 mg/kg B.W. doses of ginseng. The tested doses were given to rabbits every other day for 12 weeks. Treatment with ginseng caused significant (P < 0:05) decrease in the concentrations of glucose, plasma asparatate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) activities, lactate dehydrogenase (LDH), gamma glutamyl transferase activity (ɣ-GT), Plasma thiobarbituric acid-reactive substances (TBARS) and bilirubin. Contrariwise, the total protein (TP), globulin and albumin was significantly increased in plasma.

Concentrations of urea. But, creatinine, cholesterol, triglycerides (TG), low-density lipoprotein (LDL) and very low density lipoprotein (VLDL) were significantly decreased, while high density lipoprotein (HDL) was increased.

**Keywords:** Ginseng, biochemical parameters, antioxidant and New-Zealand white rabbits

## Introduction

Medicinal plants are plants that generally contain constituents that have been found useful for the treatment and management of both animal and human diseases[1] . The ancient Chinese have identified 11,146 medicinal species from 383 families, and more than 400 of which are widely used throughout the world [2 ,3]. Panax ginseng (Ginseng) is a well-known herb in traditional Chinese medicine (TCM) [4]. Ginseng, called the king of all herbs, has been used as a traditional medicine for the treatment of diseases for thousands of years in East Asian countries. In the last three decades, it has become one of the most popular herbs worldwide [5]. Panax means cure for all disease, as it combines the Greek words pan meaning all and zxos meaning medicine [6]. In TCM, food and medicine are understood to share similar origin but with diverse applications and uses[7] . Thus, the Chinese commonly incorporates variety of TCM herbs into their diet to make a number of healthy food recipes that are more appealing of better taste, improved texture, and will most importantly improve one's health [8]. Ginseng, a traditional medicinal plant, embodies an important position in the oriental pharmacopeia.

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Traditionally it is used primarily for treating illness, restoring homeostasis, and promoting longevity [9], but more recently is has been identified as the most commonly used herbal for controlling CVD risk factors[10] . In koria, Panax ginseng leaves have long been used as folk medicine in the treatment of diabetes, and have been consumed[11] .

**Fig. 1: Ginseng panax. (A) Whole plant (B) roots (C) powder (D) Seeds (E) Flowers**

Panax ginseng is often referred to as an adaptogen, which suggests it has varied actions and effects on the body that support nonspecific resistance to biochemical and physical stressors, improve vitality and longevity, and enhance mental capacity[12] . many studies suggest Panax ginseng has immune-modulating activity by affecting the hypothalamic-pituitary-adrenal axis[13,12]. On the other hand, ginseng was reported to have a well recognized antioxidant ability and scavenge free radicals formed as a result of oxidative processes [14]. In vitro experiments reveal enhanced natural Killer cell activity and increased immune cell phagocytosis after ginsenoside exposure [13]. According to the World Health Organization review, ginseng saponins are thought to decrease serum prolactin, thereby increasing "libido" in male impotence[15] .Increased production of reactive oxygen species may cause disruption of the lipid layer and structural organization of the membrane, altering its fluidity and permeability. This can also lead to protein modification and may stimulate protein degradation. When the lipid molecules in the membrane are in a good state of motion, there will be less fluorescence polarization, indicating higher membrane fluidity[16] . Ginseng utlize as a protector to the cells from damagedd muscles. This protection affects the mitochondrial function and dimmishes protein oxidation. The administration of several grams of ginseng daily increases the ability of the body to maintain its antioxidant status. Furthermore, lipid levels such as LDL-cholesterol are lowered [17]. [18]. In addition, more studies indicated the effect of Panax ginseng on lipid metabolism and oxidative stress in human by decreasing the total serum cholesterol, triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), malondialdhyde (MDA), superoxide dismutase (SOD) and catalase (CAT). These findings supported that ginseng have hypolipidemic potential [18].

## Material and Methods

Ginseng was purchased from public market for medicinal herbs in Al-Bayda city. All other chemicals used in the experiment were of analytical grade. Mature male New Zealand White rabbits age of 6 months and initial weight of (1.891 ± 27.6 Kg) were used. Animals were individually housed in cages and weighed weekly throughout 3-months experimental period. Feed and water were provided ad libtum. Rabbits fed pellets which consisted of 30 % berseem (Trifolium alexandrinum) hay, 25 % yellow corn, 26.2% wheat bran, 14 % soybean meal, 3 % molasses, 1 % $CaCl_2$, 0.4 % NaCl, 0.3 % mixture of minerals and vitamins, and 0.1 % methionine. The vitamin and mineral premix per kg contained the following IU/gm for vitamins or minerals: vit A-4000,000, vit D3-5000, 000, vit E-16,7 g, K0.67 g, vit B1-0.67 g, vit B2-2 g, B6-0.67 g, B12-0.004 g, B5-16.7 g, Pantothinc acid-6.67 g, Biotein-0.07 g, Folic acid-1.67 g, Choline chloride400 g, Zn-23.3 g, Mn-10 g, Fe-25 g, Cu-1.67 g, I-0.25 g, Se-0.033 g, and Mg-133.4 g (Rabbit premix produced by Holland Feed Inter. Co.). The chemical analysis of the pellets[19] showed that they contained 15.8 % crude protein, 11.3 % crude fiber, 3.7 % ether extract, 7.2 % ash, 92.9 % organic matter and 62.4 % nitrogen free extract % as DM basis. Ten mature male rabbits were randomly divided into couple equal groups (each five rabbits): Group I: Rabbits were used as control and received an equivalent volume of the vehicle (corn oil) alone by oral gavage daily for 12 successive weeks. Group II: Rabbits were treated with ginseng. Ginseng was given daily by gavage at a dose of 100 mg/kg B.W [20,21] which dissolved in corn oil for 12 successive weeks.

At the end of the experimental period, all rabbits were weighed then sacrificed under ether

anesthesia. Blood samples were collected in clean dry centrifuge tubes. Plasma was separated by centrifugation at 3000 rpm for 10 minutes and then quickly frozen at -20°c for biochemical parameters analysis.

Stored plasma samples were analyzed for total protein (TP) by the Biuret method according to [22]. Albumin (A) concentration was determined by the method of [23]. Plasma glucose, urea and creatinine concentrations were measured by the method of [24], Patton and Crouch [25] and Bishop et al[26], respectively. Plasma total bilirubin was measured using the method of Pearlman and Lee [27]. Plasma concentrations of cholesterol and triglycerides (TG) were determined according to the methods of Knight et al[28], Watson and Fossati and Principe (1982)[29,30] respectively. High-density lipoprotein (HDL) was determined according to the methods of Cooper et al.[31]. Low-density lipoprotein (LDL) was determined by the calculation (cholesterol-(TG/5+HDL). Very low-density lipoprotein (VLDL) was calculated by dividing the values of TG by factor of 5.

The activities of plasma aspartate transaminase (AST; EC 2.6.1.1) and alanine transaminase (ALT; EC 2.6.1.2) were assayed by the method of Reitman and Frankel [32]. Alkaline phosphatase (AlP; EC 3.1.3.1) activity was determined in plasma according to the method of Principato [33]. Lactate dehydrogenase (LDH EC 1.1.1.27) activity was determined by the method of Weóblewski[34] . Plasma thiobarbituric acid-reactive substances (TBARS) were measured by the method of Tappel and Zalkin [35].

## Result and Discussion

Table 1 showed the overall means of the activities of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (AlP), gamma glutamyl transferase activity (ɣ-GT), Lactate dehydrogenase (LDH), Plasma thiobarbituric acid-reactive substances (TBARS) and bilirubin in blood plasma as affected by treatment with ginseng throughout the 12-week experimental period. Treatment with ginseng resulted in significant ($P<0.05$) decrease in the activities of blood plasma AST and ALT, (ɣ-GT) , LDH,TBARS and bilirubin while ALP were significantly ($P<0.05$) increased compared with control group. Tables 2 The mean values of plasma total protein (TP), albumin (A), globulin (G), bilirubin, urea, creatinine and glucose after 3 months experimental period are shown in Table 2 . Treatment with ginseng increase plasma levels of TP, A and G, while decrease glucose, bilirubin, urea and creatinine in male rabbits. Tables 3 illustrated the effect of ginseng on the levels of total cholesterol (TC), triglyceride (TG), very low-density lipoprotein, high and low-density lipoprotein-cholesterol (HDL-c and LDL-c) in blood plasma of male rabbits. The levels of, TC, TG,and LDL-c were significantly ($P<0.05$) deceased , while HDL-c, were significantly ($P<0.05$) increased in plasma of rabbits treated with ginseng as compared with control group.

**Table 1: Changes in the activities of plasma enzyme and the level of thiobarbituric acid-reactive substances (TBARS) during treatment of male rabbits with 100 mg/kg doses of ginseng**

| Parameters | Animal Groups | |
|---|---|---|
| | Control | Ginseng |
| **AST (U/L)** | $41.23 \pm 1.652^{a}$ | $30.41 \pm 1.823^{b}$ |
| **ALT (U/L)** | $44.06 \pm 1.149^{b}$ | $37.43 \pm 1.088^{c}$ |
| **ALP (U/L)** | $139.24 \pm 2.869^{b}$ | $158.36 \pm 3.712^{a}$ |
| **ɣ-GT (U/L)** | $7.35 \pm 0.080^{b}$ | $6.69 \pm 0.224^{c}$ |
| **LDH** | $604.01 \pm 18.006^{a}$ | $477.69 \pm 19.593^{b}$ |
| **Bilirubin (mg/dl)** | $1.52 \pm 0.019^{b}$ | $1.39 \pm 0.029^{c}$ |
| **TBARS (nmol/ml)** | $0.694 \pm 0.021^{a}$ | $0.501 \pm 0.038^{a}$ |

Values are means ± SEM of 5 rabbits in each group. Mean with different letters **(a- d)** are significantly difference ($p \leq 0.05$) at same raw. Mean with the same letters (a-d) are non-significantly difference ($p \geq 0.05$).

AST, aspartate amino transferas; ALT, alanin amino transferas; AlP, alkline phosphatase; **ɣ-GT,** gamma glutamyl transe activity; Lactate dehydrogenase, TBARS, thiobarbituric acid-reactive substances.

**Table 2: Plasma total protein (TP),globulin, albumin, glucose ,urea and creatinine during treatment of male rabbits with 100 mg/kg doses of ginseng**

| Parameters | Animal Groups | |
|---|---|---|
| | Control | Ginseng |
| TP(g/dl) | 6.74 ± 0.104[ab] | 6.91 ± 0.121[a] |
| Globulin(g/dl) | 2.82 ± 0.126[a] | 2.48 ± 0.162 [a] |
| Albumin(g/dl) | 3.92 ± 0.060 [b] | 4.43 ± 0.088[a] |
| Glucose (mg/dl) | 115.6 ± 0.503[b] | 114.2 ±0.385[c] |
| Urea (mg/dl) | 38.50 ± 0.512[a] | 35.82 ±1.075[c] |
| Creatinine(mg/dl) | 0.76 ± 0.042[b] | 0.59 ± 0.021[c] |

Values are means ± SEM of 5 rabbits in each group. Mean with different letters **(a- d)** are significantly difference ($p \leq 0.05$) at same raw. Mean with the same letters (a-d) are non-significantly difference ($p \geq 0.05$).

**Table 3: Plasma lipid and lipoprotein profiles during treatment of male rabbits with 100 mg/kg doses of ginseng**

| Parameters | Animal Groups | |
|---|---|---|
| | Control | Ginseng |
| Cho | 119.9 ± 1.562c | 113.76 ± 3.194d |
| TG | 56.49 ± 1.143c | 43.08 ± 0.906d |
| HDL | 44.45± 0.347b | 41.72± 0.653a |
| LDL | 63.73 ± 0.614c | 60.79 ± 0.638d |
| VLDL | 11.42 ± 0.201c | 10.80 ± 0.093d |

Values are means ± SEM of 5 rabbits in each group. Mean with different letters **(a- d)** are significantly difference ($p \leq 0.05$) at same raw. Mean with the same letters (a-d) are non-significantly difference ($p \geq 0.05$).

Cho., cholosterol; TG, triglycerides; HDL, high density lipoprotein; LDL, low density lipoprotein; VLDL, very low density lipoprotein.

The increase in plasma proteins of animals treated with ginseng (Table 2) is in agreement with Shin et al[36], reported that serum total protein was significantly increased in mice treated with Panax Ginseng orally once a day for 7 days. Protein measurements may reflect nutritional state, kidney diseases, and liver diseases and other diseases. These facts suggest that Panax Ginseng may act as energy source and biochemical modifier. Attele reported that the ability of Ginsenosides to target the cell membrane and freely cross it, modifying its physical properties,

interacting directly with membrane proteins and even becoming incorporating into membranes [9]. Also, Song demonstrated that Ginsan, a polysaccharide isolated from Panax Ginseng, treatment did not seem to cause hepatic injury, since serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) activities and levels of total bilirubin and serum albumin were not changed [37]. Bak reported that the essential oil extracted by supercritical $CO_2$ from the byproduct after the water extraction of red ginseng inhibited hepatic lipid peroxidation in mice with carbon tetrachloride-induced liver damage[38].

Treatment with ginseng was found to significant suppressed an increase in serum AST, ALT and GGT activities, and triglyceride and cholesterol levels induced by ginseng in rats. These findings indicate that ginseng has nephroprotective as well as hepatoprotective effect. Already there are many researchers declared that ginsenoside compounds may be responsible for its hepatoprotective effect by scavenge and destroy lipit peroxyl radicals and reactive oxygen species [39]. Previous studies showed that red ginseng at dose of 3-6 g/day for eight weeks improved the antioxidant enzymes and oxidative stress markers in healthy human [40]. And, the 8 g/day intake of red ginsengs may not improve the redox status of glutathione in human [41]. Oxidative stress represents an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense system[42],[43] .

Previous study of Bak et al. (2012) showed that red ginseng oil has a protective effect on liver damages by inducing the antioxidant enzymes activity and by inhibiting lipid peroxidation in vitro and in vivo[38]. Similarly, Hyemee demonstrated that red ginsengs suppress the level of TBARS, a lipid peroxidation biomarker compared to control using rat models. It suggests that red ginsengs have an antioxidant property, which is in an agreement to the results of the present study irrespective to the source of the ginseng[44]. Ginseng treatment significantly decreased the elevated levels of urea, creatinine and biluribin. The mechanism by which ginseng prevents induced nephrotoxicity is not known. However the phenolic acids, flavonoids and saponins are present in the PG which may have improved the kidney functions through different antioxidant properties such as free radical scavenging activity or inhibit the formation of oxidised product. There are many studies have reported that those components of ginseng have been shown to have some supportive effects including antioxidant, antiinflammatory, and anticancer effects [45]. Panax ginseng has been proved to be an effective natural substance for accelerating alcohol metabolism and enhancing liver function, which has strong effects of antioxidant, anti-inflammatory, and improvement of immunity [44]. In fact, Ginseng extract contains several groups of compounds other than Ginsenosides, such as Phenolic substances (maltol, salicylic acid,vanillic acid) with direct and indirect consequences in terms of antioxidant activity [45]. Therefore, the exact mechanism of action of Ginseng remains unclear because of the complex composition of the extract [46]. Further studies to fully investigate this potential mechanism of Ginseng are certainly warranted. The health benefit of medicinal plants usually comes from the antioxidant properties of phenolic compounds in the plant.

Studies have demonstrated that Ginseng root extracts inhibit both lipid-soluble and water-soluble antioxidant activity ex vivo, and that this antioxidant action occurs both directly through free radical scavenging and indirectly through upregulation of antioxidant enzymes leading to the prevention of DNA degradation [47]. The effect of ginseng low-molecular weight compounds in the diet on the reduction of MDA in the plasma is considered the action of phenolic compounds in the ginseng extract, increasing the activity of antioxidant enzymes. According to Zhang [48]. the water extract of ginseng inhibited the in vitro lipid peroxidation. Bak et al. reported that the essential oil extracted by supercritical $CO_2$ from the byproduct after the water extraction of red ginseng inhibited hepatic lipid peroxidation in mice with carbon tetrachloride-induced liver damage[38]. Ginseng extract has been reported to scavenge superoxide radicals, to inhibit lipid peroxidation through transition metal chelation , and to reduce the oxidative DNA damage[48].

Moreover, the current study revealed that administration of Panax ginseng to hyper-cholesterolemic rabbits for twelve weeks

produced a significant reduction in TC, TGs, LDL, and VLDL; while, a significant increase in HDL level was observed in dose-dependent manner as shown in Table 3. These results are in agreement with the work of EL-Farok who studied the effect of Panax ginseng on hypercholesterolemic patients[49], for two months and also agree with Lee who studied the effect of Panax ginseng on hyper-cholesterolemic mice for 11 weeks[50] .and also with other studies , Lipoprotein lipase (LPL) catalyzes the hydrolysis of the triacylglycerol component of circulating chylomicrons and very low density lipoproteins (VLDL), thereby providing non-esterified fatty acids and 2monoacylglycerol for tissue utilization [51,52].

The ginseng effect have been reported on TG level by decreasing and HDL-C level increasing after administration of 100-mg and 200-mg doses of ginseng but these effects were not statistically significant. The result of this study is consistent with our own study. The sample size and study duration and ginseng dosage is similar to that used in our study[53].

. Yokozawa et confirmed that blood cholesterol content decreased by promoting LDL receptor synthesis, contrary to our results[54]. On the other hand, Kang claimed that the administration of ginseng ginsenoside was not effective in lowering blood cholesterol in hypercholesterolemic rabbits, which was consistent with our results[55]. In conclusion, the disagreement in the effect of ginseng on lowering cholesterol in the blood can be attributed to the composition of ginseng extract used in the experiments, dosages, and experimental periods.

## Conclusion

Ginseng is a potent antioxidant due to its ability to attenuate the reactivity of ROS and to enhance the activities of detoxifying enzymes thereby prevent lipid peroxidation reactions. Also, ginseng treatment improvement hepatic and renal cells as well as restoration of lipid profile and glucose level.

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